

### REMARKS

Claims 60-71 are pending in this application. Applicants have cancelled claims 60-71, without prejudice, and reserves the right to prosecute the subject matter of the cancelled claims in one or more related applications.

New claims 72-100 have been added. Support for the new claims can be found in the specification as originally filed, as indicated in the table of below:

<u>New Claim(s)</u>	<u>Support in Specification</u>
72	<p>“A pharmaceutical composition comprising” (see [0023])</p> <p>“an extract from <i>Trichosanthes rosthornii</i> Harms or <i>Trichosanthes japonica</i> Regal,” (see [0021] and [0041])</p> <p>“wherein said extract is prepared by a method comprising the steps of:</p> <ul style="list-style-type: none"> <li>(a) contacting the plant with a first solvent having a polarity index greater than 2 to form a mixture;</li> <li>(b) heating the mixture to form a liquor;</li> <li>(c) concentrating the liquor to form a first syrup” (see [0026])</li> </ul>
73	<p>“further comprising the step of: (d) extracting the first syrup with a second solvent having a polarity index less than that of the first solvent to form a second syrup” (see [0027])</p>
74	<p>“further comprising the step of: (e) purifying the second syrup to obtain a compound” (see [0028])</p>
87	<p>“A pharmaceutical composition comprising” (see [0023])</p> <p>“an extract from a plant of <i>Trichosanthes</i>,” (see [0021] and [0041])</p> <p>“wherein said extract is prepared by a method comprising the steps of:</p> <ul style="list-style-type: none"> <li>(a) contacting the plant with a first solvent having a polarity index greater than 2 to form a mixture;</li> <li>(b) heating the mixture to form a liquor;</li> <li>(c) concentrating the liquor to form a first syrup; and</li> <li>(d) extracting the first syrup with a second solvent having a polarity index less than that of the first solvent to form a second syrup” (see [0026] and [0027])</li> </ul>
75, 88	<p>“extract exhibits a major peak...at a flow rate of 2.0 ml/min” (see [0035])</p>
89	<p>“plant is...<i>Trichosanthes japonica</i> Regal” (see [0041])</p>
76, 90	<p>“extract is prepared from the...seeds” (see [0042])</p>
77, 91	<p>“further comprising a pharmaceutically acceptable carrier or adjuvant” (see [0024], [0072] and [0075])</p>
78, 92	<p>“first solvent is water, a lower alkanol, or a mixture thereof” (see [0029])</p>
79, 93	<p>“first solvent is an aqueous solution of from 50% to 70% ethanol” (see</p>

	[0029])
80, 94	“second solvent is a lower alkanol, or a mixture of water and a lower alkanol” (see [0030])
81, 95	“second solvent is ethanol” (see [0030])
82, 96	“step (b) is performed at a temperature ranging from 40°C to 80°C” (see [0031])
83, 97	“method for treating hemoglobinopathies in a human subject” (see [0025])
84, 98	“hemoglobinopathies is...sickle cell anemia” (see [0051])
85, 99	“method for stimulating cell differentiation into erythrocytes” (see [0025])
86, 100	“method for inducing expression of hemoglobin gene” (see [0025])

No new matter has been added. Upon entry of these amendments, claims 72-100 will be pending.

**I. THE CLAIM OBJECTIONS SHOULD BE WITHDRAWN**

Claims 60-69 are objected to because the term “hemoglobinopathies” is misspelled.

In response, Applicants submit that claims 60-69 have been cancelled, thus rendering the objections moot. Withdrawal of the objections is respectfully requested.

**II. THE CLAIMS REJECTIONS UNDER 35 U.S.C. § 112 SHOULD BE WITHDRAWN**

Claims 60-69 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that pathological conditions associated with hemoglobinopathies “can be treated, but not prevented” (see Office Action, page 3, first paragraph, lines 5-6).

In response, Applicants submit that claims 60-69 have been cancelled, thus rendering the rejections moot. Withdrawal of the rejections is respectfully requested.

Also, Applicants submit that diabetes is not a pathological condition associated with hemoglobinopathies, thus it is irrelevant whether Applicants can show that diabetes would be completely prevented in every instance.

**III. THE CLAIMS REJECTIONS UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN**

Claims 60-69 are rejected under 35 U.S.C. § 101 allegedly because the claimed invention is not supported by either an asserted utility or a well established utility. Specifically, the Examiner alleges that utility of the claims would not be credible, since

“there is no evidence that pathological condition associated with hemoglobinopathies would be prevented” (see Office Action, page 3, last paragraph).

In response, Applicants submit that claims 60-69 have been cancelled, thus rendering the rejections moot. Withdrawal of the rejections is respectfully requested.

Also, Applicants submit that each of the new claims asserts a well established utility. In particular, new independent claims 72 and 87 are directed to a pharmaceutical composition and new independent claims 83 and 97, new independent claims 85 and 99, and new independent claims 86 and 100 are directed to a method for treating hemoglobinopathies, a method for stimulating cell differentiation into erythrocytes, and a method for inducing expression of hemoglobin gene, respectively.

Applicants believe that the Examiner’s interpretation of the term “pathological condition” is incorrect. The invention provides that, as a result of receiving the claimed composition, the human subject does not become inflicted with, *i.e.*, is prevented from acquiring, a pathological condition as a result of its underlying genetic condition. While the genetic disease (*e.g.*, hemoglobinopathies) cannot be prevented, the manifested pathological conditions from such genetic disease can be prevented, for example, by reactivating fetal hemoglobin production.

#### **IV. THE CLAIMS REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN**

Claims 60-69 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ozaki *et al.*, “Antiinflammatory effect of *Trichosanthes kirilowii* MAXIM, and its effective parts,” Biol Pharm Bull. 1996 Aug;19(8):1046-8 (hereinafter “Ozaki *et al.*,” a complete copy of which is enclosed as reference C01 in the Supplemental Information Disclosure Statement submitted herewith). Claims 60-69 are also rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,910,307 to Kwak *et al.* (hereinafter “Kwak *et al.*”). Claims 60-69 are further rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Korean Patent Publication No. 2001-0106527 to Lee *et al.* (hereinafter “Lee *et al.*,” a copy of which and a certified English translation thereof are enclosed as reference B01 in the Supplemental Information Disclosure Statement submitted herewith).

In response, Applicants submit that claims 60-69 have been cancelled, thus rendering the rejections moot. Withdrawal of the rejections is respectfully requested.

Also, Applicants submit that the new claims are not anticipated by any of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.*, as detailed below.

**1. The Legal Standard**

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *see also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989) (“The identical invention must be shown in as complete detail as is contained in the...claim.”). An anticipating reference must disclose every element of the claim and enable one skilled in the art to make the anticipating subject matter. *General Electric Co. v. Nintendo Co.*, 179 F.3d 1350, 50 U.S.P.Q.2d 1910 (Fed. Cir. 1999).

**2. The New Claims Are Not Anticipated By Ozaki *et al.*, Kwak *et al.*, or Lee *et al.***

Ozaki *et al.* discloses an extract of the fruit of *Trichosanthes kirilowii* Maxim (see Abstract); Kwak *et al.* discloses an extract of a mixture of Clematis Radix, Trichosanthes root, and Prunella Herba (see Abstract) and also separately an extract of *Trichosanthes* root (see Comparative Example at col. 7, lines 50-58); and Lee *et al.* discloses an extract of a mixture of *Gleditsia japonica* Miq., *Cimicifuga heracleifolia* Kom., *Bletilla striata*, and *Trichosanthes kirilowii* Maxim (see Abstract). However, none of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.* teach an extract from *Trichosanthes rosthornii* Harms or *Trichosanthes japonica* Regal, as recited in new claim 72. Thus, new claim 72, and its dependent claims, are not anticipated by Ozaki *et al.*, Kwak *et al.*, or Lee *et al.*

Also, none of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.* teach an extract that is made only from *Trichosanthes* plant using two different solvents. In particular, none of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.* teach preparing an extract of *Trichosanthes* by contacting the plant with a first solvent having a polarity index greater than 2, and, subsequently, extracting with a second solvent having a polarity index less than that of the first solvent, as recited in new claim 87. Instead, each of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.* discloses an extract that is made either from a *Trichosanthes* plant alone using one solvent or from a mixture of *Trichosanthes* and other non-*Trichosanthes* plants using multiple solvents. Ozaki *et al.* only discloses extracting the fruit of *Trichosanthes kirilowii* Maxim with a 50% ethanol solution

(see p.1046, col. 1, ¶4). Kwak *et al.* discloses (i) extracting a mixture of Clematis Radix, Trichosanthes root, and Prunella Herba with water or alcoholic solution, and subsequently with water saturated n-butanol or propyl alcohol (see col. 3, lines 4-15) and (ii) extracting Trichosanthes root just with water (see col. 7, lines 50-58). Lee *et al.* discloses extracting a mixture of *Gleditsia japonica* Miq., *Cimicifuga heracleifolia* Kom., *Bletilla striata*, and *Trichosanthes kirilowii* Maxim with a mixture of one or more of an ethanol aqueous solution, a methanol aqueous solution, a 1,3-butylene glycol aqueous solution, a propylene glycol aqueous solution, and a glycerin aqueous solution (see Abstract). Thus, new claim 87, and its dependent claims, are not anticipated by Ozaki *et al.*, Kwak *et al.*, or Lee *et al.*

Moreover, none of Ozaki *et al.*, Kwak *et al.*, and Lee *et al.* teach treating hemoglobinopathies, stimulating cell differentiation into erythrocytes, or inducing expression of hemoglobin gene, by administering an extract of *Trichosanthes*, as recited in new claims 83 and 97, new claims 85 and 99, and new claims 86 and 100, respectively. Thus, new claims 83, 85, 86, 97, 99 and 100, and their dependent claims, are not anticipated by Ozaki *et al.*, Kwak *et al.*, or Lee *et al.*

#### **V. THE CLAIMS REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN**

Claims 60-69 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kwak *et al.* in view of Ozaki *et al.* Specifically, the Examiner alleges that “it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to extract *Trichosanthes* with ethanol since Ozaki *et al.* teach using 50% ethanol to extract *Trichosanthes* and the extract shows antiinflammatory and analgesic activities, one of ordinary skill in the art would have been motivated to make the modifications” (see Office Action, page 6, ¶4).

In response, Applicants submit that claims 60-69 have been cancelled, thus rendering the rejections moot. Withdrawal of the rejections is respectfully requested.

Also, Applicants submit that the new claims are patentable over Kwak *et al.* in view of Ozaki *et al.*, as discussed below.

##### **1. The Legal Standard**

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the

level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." *Hartness Int'l Inc. v. Simplimatic Eng'g Co.*, 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987). An analysis under 35 U.S.C. § 103(a) "should be made explicit," and "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, 2007 WL 1237834, at \*14 and \*15, respectively (2007).

**2. The New Claims Are Patentable Over Kwak *et al.* In View Of Ozaki *et al.***

Ozaki *et al.* reports the elucidation of the antiinflammatory effect of extracts from the fruit of a single plant species, *i.e.*, *Trichosanthes kirilowii Maxim* (see Abstract). In particular, Ozaki *et al.* used the same solvent (*i.e.*, 50% ethanol) to extract the whole fruit, the seeds, and the seedless fruit since the fruit has been used as a decoction with an alcoholic drink (see p.1046, col. 1, ¶4). Therefore, there is nothing to suggest using additional solvents as the goal of Ozaki *et al.* is to study the distribution of antiinflammatory substances within the fruit.

Kwak *et al.* teaches the enhanced efficacy achieved by the synergistic effects of certain mixed plant ingredients rather than a single component (see col. 4, lines 6-12). In particular, Kwak *et al.* discloses a blending ratio of three different medicinal plants (*i.e.*, Clematis Radix, Trichosanthes root, and Prunella Herba) and a process of extraction of the mixture using a two-solvent system (*i.e.*, water or alcoholic solution followed by water saturated n-butanol or propyl alcohol) (see col. 3, lines 4-20).

Applicants submit that a person skilled in the art would have no motivation to combine the teachings of the two references to arrive specifically at the claimed invention for the following reasons.

The two references each teaches extraction from a different part of *Trichosanthes*. In particular, Ozaki *et al.* extract from the fruit of *Trichosanthes kirilowii*, whereas Kwak *et al.* extract from the root of *Trichosanthes* in a mixture with other plants. As the results of Ozaki *et al.* show, the substance(s) that produce the antiinflammatory and analgesic effects are likely to be concentrated in the seeds. A person skilled in the art would expect different parts of *Trichosanthes* to be different in composition and function, and to contain different ingredients of interest, thus requiring a different approach to extraction.

Furthermore, Kwak *et al.* discloses extracting from a mixture of plants comprising, *inter alia*, partitioning an extract of the plant mixture into two phases with water saturated n-butanol or propyl alcohol (each with limited solubility with water), and concentrating only the alcohol layer (see col. 3, lines 25-37). In contrast, Ozaki *et al.* discloses extracting from a single plant with a 50% ethanol solution (ethanol is miscible with water) (see p.1046, col. 1, ¶4). A person skilled in the art would understand that the methods of Kwak *et al.* and Ozaki *et al.* would likely yield different products because the extract concentrated from the alcohol layer of a two-phase solvent system would comprise mostly hydrophobic components from the mixture of plants, whereas an extract from an ethanol solution, as taught in Ozaki *et al.*, would comprise more hydrophilic components from the single plant.

While Ozaki *et al.* uses a single plant species and a single solvent system to produce an extract useful as an antiinflammatory/analgesic agent, Kwak *et al.* rejects the notion of extracting from a single plant (see col. 3, lines 60-61) and teaches a process involving multiple solvents to extract a mixture of three plant species (in a range of blending ratios) to produce an improved extract for the same medical uses. Following the logic of Kwak *et al.*, it would seem inconsistent to a person skilled in the art to use Kwak *et al.*'s multi-solvent process to extract only *Trichosanthes* (and using a different part of the plant).

Even assuming that there is motivation for a person skilled in the art to combine the teachings of Kwak *et al.* and Ozaki *et al.*, which there is none, Applicants submit that the references do not teach or suggest each and every element of the new claims. In particular, Kwak *et al.* and Ozaki *et al.*, either alone or together, do not teach or suggest an extract from *Trichosanthes rosthornii* Harms or *Trichosanthes japonica* Regal, as recited in new claim 72.

Also, Kwak *et al.* and Ozaki *et al.*, either alone or together, do not teach or suggest an extract from a plant of *Trichosanthes* prepared by using a first solvent having a polarity index greater than 2 and a second solvent having a polarity index less than that of the first solvent, as recited in new claim 87. Moreover, Kwak *et al.* and Ozaki *et al.*, either alone or together, do not teach or suggest treating hemoglobinopathies, stimulating cell differentiation into erythrocytes, or inducing expression of hemoglobin gene, by administering an extract of *Trichosanthes*, as recited in new claims 83 and 97, new claims 85 and 99, and new claims 86 and 100, respectively.

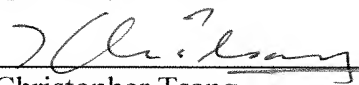
Thus, a *prima facie* case of obviousness cannot be established based on Kwak *et al.* and Ozaki *et al.*

### **CONCLUSION**

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

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Respectfully submitted,

  
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Enclosures